REMARKS

Support for the Amendments

The amendments are fully supported in the specification as filed. Support for the amendment to claim 13 ("wherein the wells comprise cells") can be found, for example, on page 9 lines 17-19. Support for the amendments in various claims to recite "computer" system are supported in claim 13 as filed. The clause "wherein the image data, the feature data, the well summary data, and the plate summary data can be retrieved from the computer system database" added to claim 13 is supported, for example, on page 8 line 30 to page 9 line 3, as well as on page 13 lines 25-27 and on page 14 lines 4-7. Thus, no new matter is added.

Title

As requested by the Patent Office, the Applicants have amended the title of the application.

Claim rejections under 35 USC 112 first paragraph

The Patent Office rejected claims 13-25 under 35 USC 112 first paragraph for failing to meet the written description requirement, based on the assertion that the claims represent new matter. The Applicants traverse this rejection.

The Patent Office asserted the following as new matter:

(a) Figure 7 is asserted to cite operator input of necessary parameters, which is not recited in claim 13 step (b). The Applicants traverse this rejection.

As an initial matter, Figure 7 provides an example of the methods of the invention. The invention is defined by the claims, not simply by what is present in Figure 7. Claim 13(b) recites "*..storing input parameters used for screening of the plate in a computer system database...*" The Patent Office acknowledges that this is supported in Figure 7, which provides an example wherein the operator inputs the parameters (also see figure legend for figure 7). Thus, there is no issue of new matter here: in fact, the Patent Office has explicitly acknowledged support for the claim in Figure 7. Further support is provided on page 9 lines 9-15. Finally, as noted on page 9 lines 12-15:

"For flexibility to handle a wide range of samples, the software next allows selection of various parameter settings used to identify nucleic, cytoplasm, different fluorescent reagents, cell selection settings, and number of cells to be analyzed. **These parameters are** ***stored in the system's database for easy retrieval for each automated run.***"

Thus, it is clear that there is no requirement that the operator must input the parameters each time the method is conducted, since it could be entered once and then stored for easy retrieval; the above recitation from the specification provides explicit support for this, and it would also be readily apparent to those of skill in the art. Therefore, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(b) Figure 7 lacks any "storing...in a database" limitation as recited in claim 13 step (b). The Applicants traverse this rejection.

Claim 13(b) recites "...iii) storing the image data in the computer system database..." Figure 7 clearly shows that the data generated can be reviewed (see 117-120), which makes clear to those of skill in the art that the data is stored in a database. Furthermore, as is clearly stated on page 13 lines 25-27:

"After a scan of the plate is complete, images and data can be reviewed with the system's image review, data review, and summary review facilities. ***All images, data, and settings from a scan are archived in the system's database for later review.***"

As further stated on page 14 lines 4-6:

"***All images and data are stored in [] the system's database for archival and retrieval or for interface with a network laboratory management information system***."

Thus, the Patent Office's assertion that "storing in a database" is new matter is baseless, and the Applicants respectfully request reconsideration and withdrawal of this rejection.

(c) Claim 13 step (b) specifies that the parameters are used for screening of the plate, but no such specificity is present in Figure 7. The Applicants traverse this rejection.

Claim 13 (b) recites "storing input parameters used for screening of the plate..." The claim clearly recites in 13(a) that the plate contains wells and that the wells comprise cells. Exemplary input parameters are noted on page 12-14 ("For flexibility to handle a wide range of samples, the software next allows selection of various parameter settings used to identify nucleic, cytoplasm, different fluorescent reagents, cell selection settings, and number of cells to be analyzed.") The specification goes on to recite at page 9 lines 15-17:

> "The system's interactive cell identification mode simplifies the selection of morphological **parameter limits such as the range of size, shape, and intensity of cells to be analyzed**."

Since the plate contains wells and the wells comprise cells, it is explicit from this portion of the specification that the parameters are used for screening of the plate. Furthermore, those of skill in the art would clearly understand that the purpose of the parameters is to screen the plate.

Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(d) The bottom of Figure 7 indicates generation of a report on a plate but does not indicate any "summary" as recited in Claim 13 step (c)(viii). The Applicants traverse this rejection.

Claim 13 (c)(viii) recites "...calculating plate summary data using the well summary data from the computer system database..", which is explicitly supported, for example, on page 13 line 25 to page 14 line 3 as follows:

> "After a ***plate scan*** is complete, images and data can be reviewed with the system's image review, data review, and ***summary review facilities***. All images, data, and settings from a scan are archived in the system's database for later review. Users can review the images alone of every cell analyzed by the system with an interactive image review procedure 117. The user can review data on a cell-by-cell basis using a combination of interactive graphs, a data spreadsheet of features measured, and images of all the fluorescence channels of a cell of interest with the interactive cell-by-cell data review procedure 118. Graphical plotting capabilities are provided in which data can be analyzed via

interactive graphs such as histograms and scatter plots. ***Users can review summary data that are accumulated and summarized for all cells within each well of a plate with an interactive well-by-well data review procedure*** 119."

And further on page 14 lines 8-15:

> "As a final phase of a complete scan, reports can be generated on one or more statistics of the measured features. ***Users can generate a graphical report of data summarized on a well-by-well basis for the scanned region of the plate using an interactive report generation procedure 120***. This report includes a ***summary*** of the statistics by well in tabular and graphical format and identification information on the sample. The report window allows the operator to enter comments about the scan for later retrieval. Multiple reports can be generated on many statistics and be printed with the touch of one button. Reports can be previewed for placement and data before being printed."

Thus, it is clear that the specification provides ample written description of the recited summaries. Thus, the Applicants respectfully request reconsideration and withdrawal of this rejection.

(e) Claim 23 recites "fluorescent agents" where page 9 recites "different fluorescent agents."

The Applicants have amended the claim to obviate this rejection, and thus respectfully request reconsideration and withdrawal of the rejection.

(f) Claims 24 and 25 recite a ratio of fluorescent intensity limitation without further limitation regarding cytoplasmic mask or an average of cell nucleus fluorescent intensity, as on pages 11-12. Specifically, the Patent Office states that "ratios of fluorescent intensities are only disclosed regarding comparison of the cytoplasmic mask to average fluorescent intensity within the cell nucleus." The Applicants traverse this rejection.

The Applicants note that the disclosure on pages 11-12 is exemplary. On page 12 lines 22-25, the specification states:

> "Features 5-9 have been developed specifically to provide measurements of a cell's fluorescent molecules within the local

cytoplasmic region of the cell and the ***translocation*** (i.e. movement) of fluorescent molecules **from the cytoplasm to the nucleus.**"

Further, on page 12 lines 30-31:

"Quantification of the difference between these two sub-cellular compartments provides a measure of cytoplasm-nuclear translocation (feature 9)."

Finally, on page 19 lines 3-15:

"Those skilled in the art will ***recognize a wide variety of distinct screens that can be developed based on the disclosure provided herein***. There is a large and growing list of known biochemical and molecular processes in cells that involve ***translocations or reorganizations of specific components within cells***. The signaling pathway from the cell surface to target sites within the cell involves the ***translocation of plasma membrane-associated proteins to the cytoplasm***. For example, it is known that one of the src family of protein tyrosine kinases, pp60c-src (Walker et al (1993), *J. Biol. Chem.* 268:19552-19558) translocates from the plasma membrane to the cytoplasm upon stimulation of fibroblasts with platelet-derived growth factor (PDGF). In contrast, some cytoplasmic components ***translocate*** from the ***cytoplasm to the plasma membrane*** upon stimulation of cells....In addition, ***specific organelles***, such as components of the cytoskeleton, nuclear envelope, chromatin, golgi apparatus, mitochondria, and endosomes are ***reorganized*** in response to specific stimuli."

Thus, the specification clearly provides explicit examples of using ratios of fluorescent intensities in the cytoplasm-nucleus translocation asays, as acknowledged by the Patent Office. The specification clearly provides disclosure of other translocation and reorganization assays, such as translocation between cytoplasm and plasma membrane, that can be developed based on these teachings. It would thus be clear to those of skill in the art that the Applicants had possession of other translocation assays as of the filing date of the invention, and that, as in the cytoplasm-nucleus translocation assays, ratios of fluorescent intensities could be used in these other translocation assays.

Thus, the specification provides adequate written description for ratios of fluorescent intensities, and therefore the Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim rejections under 35 USC 112 second paragraph

The Patent Office rejected claims 13-25 under 35 USC 112 second paragraph as being indefinite. The Applicants traverse this rejection, but have nonetheless amended the claims to accelerate prosecution of this application. The Applicants further note that the amendment to recite "computer" system does not serve to limit the scope of the claim, as the term "system" recited in Claim 13 steps (b) and (c) clearly referred back to "computer system" as recited in the preamble.

Therefore, the Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim rejections based on 35 USC 102(e)

The Patent Office rejected claims 13-24 under 35 USC 102(e) over Sabry (US Pat. No. 6,615,141). The Applicants traverse this rejection.

The Applicants note that the earliest claimed priority date for Sabry is May 14, 1999. The present application is a continuation of U.S. Patent Application Ser. No. 09/293,209 filed April 16, 1999, which is a divisional of 08/810,983 filed February 27, 1997. Thus, the priority date of the present application is February 27, 1997, which removes the Sabry patent as a proper anticipatory reference.

Therefore, the Applicants respectfully request reconsideration and withdrawal of this rejection.

Information Disclosure Statement

The Applicants are herewith submitting a further copy of PTO Form 1449 as requested by the Patent Office, together with the return receipt postcard stamped by the Patent Office on December 13, 2001 noting that the Patent Office received both the Form 1449 and the cited references.

If there are any questions or comments regarding this Response, the Patent Office is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

Date: 3/25/05

David S. Harper
Registration No. 42,636

McDonnell Boehnen
Hulbert & Berghoff, Ltd.
300 South Wacker Drive
Chicago, IL 60606

Telephone: 312-913-0001
Facsimile: 312-913-0002